



Complete Summary

GUIDELINE TITLE

Uncomplicated urinary tract infections in adults. In: Guidelines on the management of urinary and male genital tract infections.

BIBLIOGRAPHIC SOURCE(S)

Uncomplicated urinary tract infections in adult. In: Grabe M, Bishop MC, Bjerklund-Johansen TE, Botto H, Çek M, Lobel B, Naber KG, Palou J, Tenke P. Guidelines on the management of urinary and male genital tract infections. Arnhem, The Netherlands: European Association of Urology (EAU); 2008 Mar. p. 11-40. [152 references]

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [July 08, 2008 – Fluoroquinolones \(ciprofloxacin, norfloxacin, ofloxacin, levofloxacin, moxifloxacin, gemifloxacin\)](#): A BOXED WARNING and Medication Guide are to be added to the prescribing information to strengthen existing warnings about the increased risk of developing tendinitis and tendon rupture in patients taking fluoroquinolones for systemic use.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **

SCOPE

METHODOLOGY - including Rating Scheme and Cost Analysis

RECOMMENDATIONS

EVIDENCE SUPPORTING THE RECOMMENDATIONS

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

CONTRAINDICATIONS

QUALIFYING STATEMENTS

IMPLEMENTATION OF THE GUIDELINE

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

SCOPE

DISEASE/CONDITION(S)

Uncomplicated urinary tract infection (UTI), e.g.:

- Acute cystitis
- Acute pyelonephritis

Note: The distinction between uncomplicated and complicated UTI is important. In contrast to an uncomplicated UTI, *a complicated UTI is an infection associated with a condition that increases the risks of acquiring an infection or of failing therapy.* At the time of presentation with an acute onset of urinary tract symptoms, it is usually not possible to classify definitively patients as having a complicated or an uncomplicated UTI. See the original guideline document for a list of factors that suggest potential complicated UTI.

GUIDELINE CATEGORY

Diagnosis
Management
Prevention
Screening
Treatment

CLINICAL SPECIALTY

Family Practice
Infectious Diseases
Internal Medicine
Obstetrics and Gynecology
Urology

INTENDED USERS

Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

- To assist urologists and physicians from other medical specialties in their daily practice
- To provide recommendations on the diagnosis and management of uncomplicated urinary tract infections in adults

TARGET POPULATION

Adults (including pregnant women) with uncomplicated urinary tract infections (UTIs)

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Screening

1. Physical examination
2. Urinalysis (dipstick, including white and red blood cells, nitrites)
3. Colony counts
4. Imaging, as indicated (ultrasound of the upper urinary tract; computed tomography (CT), excretory urogram, or dimercaptosuccinic acid (DMSA) scan in patients who remain febrile after 72 hours of treatment)
5. Gynecologic evaluation in post-menopausal women
6. Urological evaluation in men
7. Indications for screening (not generally recommended)

Treatment/Management

1. Antimicrobial treatment: trimethoprim (TMP) or TMP-sulphamethoxazole (SMX) as first-line empirical therapy, fluoroquinolones, fosfomycin trometamol, pivmecillinam, nitrofurantoin, beta-lactam antibiotics, beta-lactamase inhibitor (BLI)
2. Hospitalization with parenteral fluoroquinolone, third-generation cephalosporin, or amino/acylaminopenicillin plus a BLI in severe cases
3. Treatment duration: single dose, short course (4-7 days), longer courses
4. Treatment by population: pre-menopausal women, pregnant women, post-menopausal women, young men, asymptomatic patients with bacteriuria
5. Follow-up (dipstick urinalysis, post-treatment cultures and antimicrobial susceptibility testing, if indicated)

Prevention of Recurrence

1. Prophylactic antimicrobials at bedtime or after intercourse
2. Intravaginal oestriol in post-menopausal women
3. Prophylactic alternative therapies: immunotherapy, probiotic therapy, acidification, cranberry juice
4. Prevention in pregnant women

MAJOR OUTCOMES CONSIDERED

- Rate of post-treatment bacteriuria
- Time to bacterial clearance
- Occurrence of bacterial resistance
- Overall cure rate
- Incidence of adverse events from treatment
- Rate of recurrent urinary tract infection (RUTI)
- Change of rate of recurrence with prophylaxis
- Mortality and complication rates from treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

General Search Strategy

Up until 2007, the main strategy was to rely on the guidelines group members' knowledge and expertise on the current literature assuming that all, or almost all, relevant information would be captured.

In updates produced from 2008 onwards, a structured literature search will be performed for all guidelines but this search will be limited to randomized controlled trials and meta-analyses, covering at least the past three years, or up until the date of the latest text update if this exceeds the three-year period. Other excellent sources to include are other high-level evidence, Cochrane review and available high-quality guidelines produced by other expert groups or organizations. If there are no high-level data available, the only option is to include lower-level data. The choice of literature will be guided by the expertise and knowledge of the Guidelines Working Group.

Specific Strategy for This Guideline

For literature review, PubMed was searched for published meta-analyses, which were used as far as available. Otherwise there was a non-structured literature review process by the group members. Each member was responsible for one chapter (reporter).

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)
Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Ia Evidence obtained from meta-analysis of randomized trials

Ib Evidence obtained from at least one randomized trial

IIa Evidence obtained from at least one well-designed controlled study without randomization

IIb Evidence obtained from at least one other type of well-designed quasi-experimental study

III Evidence obtained from well-designed non-experimental studies, such as comparative studies, correlation studies and case reports

IV Evidence obtained from expert committee reports or opinions or clinical experience of respected authorities

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Consensus Development Conference)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

General Methods Used to Formulate the Recommendations

- The first step in the European Association of Urology (EAU) guidelines procedure is to define the main topic.
- The second step is to establish a working group. The working groups comprise about 4-8 members, from several countries. Most of the working group members are academic urologists with a special interest in the topic. Specialists from other medical fields (radiotherapy, oncology, gynaecology, anaesthesiology etc.) are included as full members of the working groups as needed. In general, general practitioners or patient representatives are not part of the working groups. Each member is appointed for a four-year period, renewable once. A chairman leads each group.
- The third step is to collect and evaluate the underlying evidence from the published literature.
- The fourth step is to structure and present the information. All main recommendations are summarized in boxes and the strength of the recommendation is clearly marked in three grades (A-C), depending on the evidence source upon which the recommendation is based. Every possible effort is made to make the linkage between the level of evidence and grade of recommendation as transparent as possible.

Specific Methods Used for This Guideline

The members of the Urinary Tract Infection (UTI) Working Group of the EAU Health Care Office established the first version of these guidelines in several consensus conferences. The members of the current UTI Working Group of the

EAU Guidelines Office updated the guidelines in several consensus conferences thereafter. The first draft of each chapter was sent to the committee members asking for comments, which were then considered, discussed and incorporated accordingly.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

- A. Based on clinical studies of good quality and consistency addressing the specific recommendations and including at least one randomized trial
- B. Based on well-conducted clinical studies, but without randomized clinical studies
- C. Made despite the absence of directly applicable clinical studies of good quality

COST ANALYSIS

A study found screening for UTIs in pregnancy to be cost effective when the prevalence of bacteriuria was >2%.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The formal agreement to each updated chapter was achieved by the European Association of Urology (EAU) working group at three plenary meetings: the first in Paris on 10 December 2004, the next in Istanbul on 15 March 2005, and finally in Florence on 22 October 2005. Each chapter was reviewed by three committee members (editorial group) for consistency and compatibility in two editorial meetings: one meeting took place in Straubing, 22-24 April 2005, and one in Stavern, 9-11 Sept 2005, and the chapters were revised accordingly.

There is no formal external review prior to publication. The Appraisal of Guidelines for Research and Evaluation (AGREE) instrument was used to analyse and assess a range of specific attributes contributing to the validity of a specific clinical guideline.

The AGREE instrument, to be used by two to four appraisers, was developed by the AGREE collaboration (www.agreecollaboration.org) using referenced sources for the evaluation of specific guidelines. (See the "Availability of Companion Documents" field for further methodology information).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The following is a summary of the recommendations for uncomplicated urinary tract infections in adults. Refer to the original guideline for more detailed recommendations and discussion.

Levels of evidence (**Ia-IV**) and grades of recommendation (**A-C**) are defined at the end of the "Major Recommendations" field.

Definition of Uncomplicated Urinary Tract Infection (UTI)

Acute, uncomplicated UTIs in adults include episodes of acute cystitis and acute pyelonephritis in otherwise healthy individuals. These UTIs are seen mostly in women who have none of the factors known to increase the risk of complications or of treatment failure.

Acute Uncomplicated Cystitis in Pre-menopausal, Non-pregnant Women

Besides physical examination, urinalysis (e.g., using a dipstick method), including the assessment of white and red blood cells and nitrites, is recommended for routine diagnosis (**B**). Colony counts $\geq 10^3$ colony forming units (cfu) uropathogen/mL are considered to be a clinically relevant bacteriuria (**IIb**).

Short courses of antimicrobials are highly effective and are desirable because of the improved compliance that they promote, their lower cost and lower frequency of adverse reactions. Single-dose therapy (with some exceptions) is generally less effective than the same antibiotic used for a longer duration. However, with most suitable antimicrobials, there is little to be gained from treatment given beyond 3 days and the risk of adverse events is higher (**IaA**).

Trimethoprim (TMP) or TMP-sulphamethoxazole (SMX) can only be recommended as first-line drugs for empirical therapy in communities with rates of uropathogen resistance to TMP of less than 20% (**IbA**). Otherwise, fluoroquinolones, fosfomycin trometamol, pivmecillinam and nitrofurantoin are recommended as alternative oral drugs for empirical therapy. However, in some areas, the rate of fluoroquinolone-resistant *Escherichia coli* (*E. coli*) is also increasing.

Urinalysis, including a dipstick method, is sufficient for routine follow-up. Post-treatment cultures in asymptomatic patients may not be indicated. In women whose symptoms do not resolve, or which resolve and then recur within 2 weeks, urine culture and antimicrobial susceptibility testing should be performed (**IVC**).

Acute Uncomplicated Pyelonephritis in Pre-menopausal, Non-pregnant Women

Acute pyelonephritis is suggested by flank pain, nausea and vomiting, fever (>38 degrees C), or costovertebral angle tenderness. It may occur in the absence of cystitis symptoms (e.g., dysuria, frequency). Besides physical examination, urinalysis (e.g., using a dipstick method), including the assessment of white and red blood cells and nitrites, is recommended for routine diagnosis (**C**). Colony counts $\geq 10^4$ cfu uropathogen/mL can be considered to be a clinically relevant bacteriuria (**IIb**).

An evaluation of the upper urinary tract with ultrasound should be performed to rule out urinary obstruction or renal stone disease (**C**). Additional investigations, such as an unenhanced helical computed tomography (CT), an excretory urogram, or dimercaptosuccinic acid (DMSA) scan, should be considered if the patients

remain febrile after 72 hours of treatment to rule out further complicating factors (e.g., urolithiasis, renal or perinephric abscesses). (**C**).

As first-line therapy in mild cases, an oral fluoroquinolone for 7 days is recommended in areas where the rate of fluoroquinolone-resistant *E. coli* is still low (<10%) (**IbA**). If a Gram-positive organism is seen on the initial Gram stain, an aminopenicillin plus a beta-lactamase inhibitor (BLI) could be recommended (**IIbB**). More severe cases of acute uncomplicated pyelonephritis should be admitted to hospital and treated according to the patient's condition parenterally with a fluoroquinolone (ciprofloxacin or levofloxacin), a third-generation cephalosporin or an amino/acylaminopenicillin plus a BLI according to the local susceptibility pattern (**IIbB**). With improvement, the patient can be switched to an oral regimen using a fluoroquinolone or TMP-SMX (if active against the infecting organism) to complete the 1- or 2-week course, respectively (**IIbB**). In areas with increased resistance rate of *E. coli* against fluoroquinolones and in situations in which fluoroquinolones are contraindicated (e.g., pregnancy, lactating women, adolescence), a second- or third-generation oral cephalosporin is recommended (**IIbB**).

Routine post-treatment cultures in an asymptomatic patient may not be indicated; routine urinalysis using a dipstick method is sufficient (**IIbB**). In women whose symptoms of pyelonephritis resolve but then recur within 2 weeks, it is important to carry out a repeat urine culture, antimicrobial susceptibility testing, and an appropriate investigation to rule out urinary tract abnormalities (**C**).

Recurrent (Uncomplicated) UTIs in Women

Recurrent UTIs (RUTIs) are common among young, healthy women, even though they generally have anatomically and physiologically normal urinary tracts. The following prophylactic antimicrobial regimens are recommended:

- Long-term, low-dose prophylactic antimicrobials taken at bedtime (**IaA**)
- Post-intercourse prophylaxis for women in whom episodes of infection are associated with sexual intercourse (**IbA**)
- A patient-initiated treatment may also be suitable for management of RUTIs in well-informed, young women (**IIaB**).

Prophylactic alternative methods include immunotherapy (**IaB**) and probiotic therapy (**IIaC**), acidification (**IIaC**), and cranberry juice (**IIaC**). These regimens are not yet as effective as antimicrobial prophylaxis, though directly comparative studies have not been performed.

UTIs in Pregnancy

Urinary tract infections are common during pregnancy. Most women acquire bacteriuria before pregnancy, while 20-40% of women with asymptomatic bacteriuria will develop pyelonephritis during pregnancy. Treatment of asymptomatic bacteriuria lowers this risk (**IIa**).

Most symptomatic UTIs in pregnant women present as acute cystitis. Short-term therapy is not as established as in non-pregnant women. For a recurrent UTI, low-

dose cephalexin (125-250 mg) or nitrofurantoin (50 mg) at night is recommended for prophylaxis against re-infection (**IbA**). Post-intercourse prophylaxis may be an alternative approach (**IbA**).

For acute pyelonephritis, second- or third-generation cephalosporins, an aminoglycoside, or an aminopenicillin plus a BLI may be recommended antibiotics (**IIbB**). During pregnancy, quinolones, tetracyclines and TMP are contraindicated in the first trimester, while sulphonamides should not be used in the last trimester (**IIbB**). In cases of delayed defervescence and upper tract dilatation, a ureteral stent may be indicated and antimicrobial prophylaxis should be considered until delivery (**IIbB**).

UTIs in Post-menopausal Women

In acute cystitis, the antimicrobial treatment policy in post-menopausal women is similar to that in pre-menopausal women. However, short-term therapy in post-menopausal women is not as well documented as that in younger women. In the case of a recurrent UTI, urological or gynaecological evaluation should be performed in order to eliminate a tumour, obstructive problems, detrusor failure or a genital infection (**IIIB**).

In post-menopausal women with a recurrent UTI, therapy with intravaginal oestriol is able to reduce significantly the rate of recurrences (**IbA**). For the remainder of patients, an antimicrobial prophylactic regimen should be recommended in addition to hormonal treatment (**IIIB**).

For acute pyelonephritis, the same treatment modalities are recommended as for pre-menopausal, non-pregnant women (see the section "Acute Uncomplicated Pyelonephritis in Pre-menopausal, Non-pregnant Women," above).

Acute Uncomplicated UTIs in Young Men

Only a small number of 15 to 50-year-old men suffer from acute uncomplicated UTI. Such men should receive, as minimum therapy, a 7-day antibiotic regimen (**IIaB**). Most men with febrile UTI have a concomitant infection of the prostate, as measured by transient increases in serum PSA and prostate volume (**IIa**). Urological evaluation should be carried out routinely in adolescents and men with febrile UTI, pyelonephritis, recurrent infections, or whenever a complicating factor is suspected (**IIIB**). A minimum treatment duration of 2 weeks is recommended (**IIIB**), preferably with a fluoroquinolone since prostatic involvement is frequent.

Asymptomatic Bacteriuria

Asymptomatic bacteriuria is common. Populations with structural or functional abnormalities of the genitourinary tract may have an exceedingly high prevalence of bacteriuria, but even healthy individuals frequently have positive urine cultures. Asymptomatic bacteriuria is seldom associated with adverse outcomes. Screening for, or treatment of, asymptomatic bacteriuria is not recommended for the following persons:

- Pre-menopausal, non-pregnant women (**IbA**)

- Diabetic women (**IbA**)
- Older persons living in community (**IIaB**)
- Elderly institutionalized subjects (**IIaB**)
- Persons with spinal cord injury (**IIaB**)
- Catheterized patients while the catheter remains *in situ* (**IbA**)

Screening for asymptomatic bacteriuria and treatment is recommended only for selected groups where benefit has been shown: pregnant women (**IbA**); before transurethral resection of the prostate (TURP) (**IbA**) and other traumatic urological interventions (**IIIB**). Antimicrobial therapy should be initiated shortly before the procedure (**IIIB**).

Definitions:

Levels of Evidence

Ia Evidence obtained from meta-analysis of randomized trials

Ib Evidence obtained from at least one randomized trial

IIa Evidence obtained from at least one well-designed controlled study without randomization

IIb Evidence obtained from at least one other type of well-designed quasi-experimental study

III Evidence obtained from well-designed non-experimental studies, such as comparative studies, correlation studies and case reports

IV Evidence obtained from expert committee reports or opinions or clinical experience of respected authorities

Grades of Recommendation

- A. Based on clinical studies of good quality and consistency addressing the specific recommendations and including at least one randomized trial
- B. Based on well-conducted clinical studies, but without randomized clinical studies
- C. Made despite the absence of directly applicable clinical studies of good quality

CLINICAL ALGORITHM(S)

The original guideline document contains a clinical algorithm for clinical management of acute pyelonephritis.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate diagnosis and management of uncomplicated urinary tract infections (UTIs) in adults

POTENTIAL HARMS

- Side effects from treatment
- Increased side effects with longer-duration treatment
- Development of antimicrobial resistance

CONTRAINDICATIONS

CONTRAINDICATIONS

- Fluoroquinolones are contraindicated in pregnant and lactating women.
- During pregnancy, quinolones, tetracyclines and trimethoprim are contraindicated in the first trimester, while sulphonamides should not be used in the last trimester.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The purpose of these texts is not to be proscriptive in the way a clinician should treat a patient but rather to provide access to the best contemporaneous consensus view on the most appropriate management currently available. European Association of Urology (EAU) guidelines are not meant to be legal documents but are produced with the ultimate aim to help urologists with their day-to-day practice.
- The EAU believe that producing validated best practice in the field of urology is a very powerful and efficient tool in improving patient care. It is, however, the expertise of the clinician which should determine the needs of their patients. Individual patients may require individualized approaches which take into account all circumstances and treatment decisions often have to be made on a case-by-case basis.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The European Association of Urology (EAU) Guidelines long version (containing all 19 guidelines) is reprinted annually in one book. Each text is dated. This means that if the latest edition of the book is read, one will know that this is the most

updated version available. The same text is also made available on a CD (with hyperlinks to PubMed for most references) and posted on the EAU websites Uroweb and Urosource (www.uroweb.org/professional-resources/guidelines/ & <http://www.urosource.com/diseases/>).

Condensed pocket versions, containing mainly flow-charts and summaries, are also printed annually. All these publications are distributed free of charge to all (more than 10,000) members of the Association. Abridged versions of the guidelines are published in European Urology as original papers. Furthermore, many important websites list links to the relevant EAU guidelines sections on the association websites and all, or individual, guidelines have been translated to some 15 languages.

IMPLEMENTATION TOOLS

Clinical Algorithm
Pocket Guide/Reference Cards

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Uncomplicated urinary tract infections in adult. In: Grabe M, Bishop MC, Bjerklund-Johansen TE, Botto H, Çek M, Lobel B, Naber KG, Palou J, Tenke P. Guidelines on the management of urinary and male genital tract infections. Arnhem, The Netherlands: European Association of Urology (EAU); 2008 Mar. p. 11-40. [152 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2008 Mar

GUIDELINE DEVELOPER(S)

European Association of Urology - Medical Specialty Society

SOURCE(S) OF FUNDING

European Association of Urology

GUIDELINE COMMITTEE

Management of Urinary and Male Genital Tract Infections Guidelines Writing Panel

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: M. Grabe (*Chairman*); M.C. Bishop; T.E. Bjerklund-Johansen; H. Botto; M. Çek; B. Lobel; K.G. Naber; J. Palou; P. Tenke

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All members of the Management of Urinary and Male Genital Tract Infections guidelines writing panel have provided disclosure statements of all relationships which they have and which may be perceived as a potential source of conflict of interest. This information is kept on file in the European Association of Urology Central Office database. This guidelines document was developed with the financial support of the European Association of Urology (EAU). No external sources of funding and support have been involved. The EAU is a non-profit organisation and funding is limited to administrative assistance, travel, and meeting expenses. No honoraria or other reimbursements have been provided.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [European Association of Urology Web site](#).

Print copies: Available from the European Association of Urology, PO Box 30016, NL-6803, AA ARNHEM, The Netherlands.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- EAU guidelines office template. Arnhem, The Netherlands: European Association of Urology (EAU); 2007. 4 p.
- The European Association of Urology (EAU) guidelines methodology: a critical evaluation. Arnhem, The Netherlands: European Association of Urology (EAU); 18 p.

The following is also available:

- Management of urinary and male genital tract infections. 2008, Ultra short pocket guidelines. Arnhem, The Netherlands: European Association of Urology (EAU); 2008 Mar. 17 p.

Print copies: Available from the European Association of Urology, PO Box 30016, NL-6803, AA ARNHEM, The Netherlands.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on September 5, 2008. The information was verified by the guideline developer on December 8, 2008.

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